DJC RIP CHL

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
FISH & RICHARDSON P.C.
Attn. Leber, Celia H.
225 Franklin Street
Boston, Massachusetts 02110-2804
UNITED STATES OF AMERICA

ACTION DUE Pay fees
DUE DATE 12.8.03
INITIALS mlk

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

Applicant's or agent's file reference 07588-008W01	Date of mailing *(day/month/year)* 24/10/2003
International application No. PCT/US 01/46047	**PAYMENT DUE** within 45 ~~months~~/days from the above date of mailing
Applicant VIACELL, INC.	International filing date *(day/month/year)* 25/10/2001

1. This International Searching Authority

(i) considers that there are 04 *(number of)* inventions claimed in the international application covered by the claims indicated ~~below~~/on the extra sheet:

and ~~it considers that~~ the international application does not comply with the requirements of unity of invention (Rules ~~13.1 and 13.2~~) for the reasons indicated below/on the extra sheet:

Docketed By Practice System
Fee invite due 12.8.03
TRANSFERRED - PLS. FORWARD ASAP
Initials: JMG

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FISH & RICHARDSON, P.C.
BOSTON OFFICE

(ii) [X] has carried out a partial international search (see Annex) [ ] will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

See annex, first group of inventions

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby **invited,** within the time limit indicated above, to pay the amount indicated below:

EUR 945,00	x	03	=	EUR 2.835,00
Fee per additional invention		number of additional inventions		total amount of additional fees

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. [X] Claim(s) Nos. See annex have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Joëlle Gerber

Form PCT/ISA/206 (July 1992)

INVITATION TO PAY ADDITIONAL FEES

International application No.
PCT/US 01/46047

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1, 18, 26, 27 complete; 6, 8-17, 19-25, 28-30, 34-36 partially

   Method for the improvement in function of the central nervous system in a subject comprising administering an aliquot of cells derived from umbilical cord blood. Excluding the subject matter of inventions 2-4.

2. Claims: 2 complete; 4-6, 8-17, 19-25, 28-30, 34-36 partially

   Method for the improvement in function of the central nervous system in a subject comprising administering an aliquot of stem cells derived from blood. Excluding the subject matter of inventions 1,3,4.

3. Claims: 3, 7, 31-33 complete; 4-6, 8-17, 19-24, 28-30, 34-36 partially

   Method for the improvement in function of the central nervous system in a subject comprising administering an aliquot of cells derived from blood in combination with a growth factor. Excluding the subject matter of inventions 1,2,4.

4. Claims: 37-41

   Method of improving central nervous system function of a patient comprising:
   1) obtaining an aliquot of a predetermined population of cells by: a) introducing starting sample of cells into growth medium, b) causing the cells of the selected population to divide, c) contacting the starting cells with a selection element for the target population to select them from other cells in the medium and
   2) administering said aliquot to the patient

The problem underlying the present invention is the treatment of malfunctions of the central nervous system (i.e. Head trauma, Parkinson disease, Alzheimer's disease, Huntington's disease, ALS, MS, Tay-Sacks, cerebral palsy, cerebral stroke or asphyxiation) (see description page 1, lines 10-16).
As solution to this problem several compositions comprising cells derived from blood (either umbilical cord blood or peripherial blood) optionally in combination with a growth factor are proposed for the improvement in the function of the central nervous system.
The common feature linking the different inventions together is the use of cells derived from blood for the improvement in function of the central nervous system in a subject.

Prior art document:
J. of Medicine (2000), vol. 31, pp.21-30 discloses the use of mononuclear cells from human umbilical cord blood in the treatment of amyotrophic lateral sclerosis (ALS) in mice (see abstract, discussion). Similar process is suggested to apply to other chronic diseases as multiple sclerosis, Huntington's disease, Alzheimer disease.(see page 29).

The common feature mentioned above is consequently not novel and therefore cannot be regarded as linking the inventions together so as to form a single general inventive concept.
As there is no other technical feature which could fulfil the role of special technical feature in the sense of rule 13 PCT, the present application lacks unity of invention, containing the subjects listed above.
Searching the plurality of inventions would have cause a major additional searching effort, initially, only the first subject was searched.
The documents cited do not represent a comprehensive search for any of the defined inventions and are to be considered in the present context only as part of the prior art pertaining to the general idea underlying the present application.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Although claims 1,6,8-30, 34-36 in relation to the first invention are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Further defect(s) under Article 17(2)(a):

Continuation of Box 3.

Claims Nos.: 1,6,8-15,19-21,25-27,29,30,34 partially

Present claims 1,6,8-15,19-21,25-27,29,30,34 relate to an extremely large number of possible methods as "improvement of the central nervous system" (claim 1); "recovery of a central nervous system trauma" (claim 12); "repair of central nervous system damage" (claim 13); "repair of central nervous system disease" (claim 14); "regeneration of central nervous system tissue" (claim 15).
Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Furthermore claims 6, 8, 9 relate to an extremely large number of possible methods as "obtaining the aliquot of cells by separating a desired cell population..." (claim 6); "obtaining a sample of cells and purifying them to obtain the aliquot" (claim 8); "obtaining a sample of cells and expanding at least a selected population of cells in the sample ex vivo to obtain the aliquot" (claim 9). Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Moreover claims 19-21, 29, 30 relate to products defined by reference to desirable characteristics or property, namely "genetic element" (claims 19-21); "cell differentiation factor" (claim 29); "neural guidance molecule" (claim 30)
The claims cover all products having these characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the method by reference to a result to be achieved "improvement of the central nervous system"; "recovery of a central nervous system trauma"; "repair of central nervous system

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

damage"; "repair of central nervous system disease"; "regeneration of central nervous system tissue". Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.
Consequently, the search for the first invention has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the methods mentioned in the example of the present application and those methods/uses specifically mentioned in claims 16-19, 22-24, 28, 35,36 and for those parts of the claims relating to the use of the products (namely cells) mentioned in claims 26, 27.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Annex t Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US 01/46047

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEN RUIFENG ET AL: "The potential for the use of mononuclear cells from human umbilical cord blood in the treatment of amyotrophic lateral sclerosis in SOD1 mice." JOURNAL OF MEDICINE (WESTBURY), vol. 31, no. 1-2, 2000, pages 21-30, XP008013824 ISSN: 0025-7850 see discussion page 29, paragraph 4 ---	1,6, 8-10, 13-15, 19,20,28
X,P	WO 01 66698 A (CRYO CELL INT ;UNIV SOUTH FLORIDA (US)) 13 September 2001 (2001-09-13) page 18 -page 19; claims 49,51,52,54,55 page 27, line 20-35 page 64 -page 71 --- -/--	1,6, 8-30, 34-36

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

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Form PCT/ISA/206 (Annex, first sheet) (July 1992)

Annex t F rm PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS
OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US 01/46047

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	KRAUS M ET AL: "Cord blood cells restore central nervous system (CNS) function in a rat-stroke model system." BLOOD, vol. 96, no. 11 Part 1, 16 November 2000 (2000-11-16), page 495a XP001109686 42nd Annual Meeting of the American Society of Hematology;San Francisco, California, USA; December 01-05, 2000 ISSN: 0006-4971 abstract	1,6, 8-10, 13-20, 26,27,35
P,X	ENDE NORMAN ET AL: "Human umbilical cord blood cells ameliorate Alzheimer's disease in transgenic mice." JOURNAL OF MEDICINE (WESTBURY), vol. 32, no. 3-4, 2001, pages 241-247, XP008013823 ISSN: 0025-7850 see discussion page 243	1,6, 8-10, 13-15, 19,20,28
P,X	ENDE NORMAN ET AL: "Human umbilical cord blood cells ameliorate Huntington's disease in transgenic mice." JOURNAL OF MEDICINE (WESTBURY), vol. 32, no. 3-4, 2001, pages 231-240, XP008013822 ISSN: 0025-7850 see discussion	1,6, 8-10, 13-15, 19,20,28
A	US 5 925 567 A (KRAUS MOREY ET AL) 20 July 1999 (1999-07-20) cited in the application figures 1,2,11; examples 4,5 column 11, paragraph 1; figure 7	1,6, 8-30, 34-36

Form PCT/ISA/206 (Annex, continuation sheet)(July 1992)

Patent Family Annex

Information on patent family members

International Application No
PCT/US 01/46047

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0166698 A	13-09-2001	AU 4346401 A	17-09-2001
		EP 1263930 A1	11-12-2002
		WO 0166698 A1	13-09-2001
		US 2002028510 A1	07-03-2002
		US 2003036729 A1	20-02-2003
US 5925567 A	20-07-1999	US 5674750 A	07-10-1997
		AU 711528 B2	14-10-1999
		CA 2221433 A1	06-04-1999
		US 2002150561 A1	17-10-2002
		US 2001036663 A1	01-11-2001
		US 6429012 B1	06-08-2002
		US 2002022216 A1	21-02-2002
		AU 4852197 A	19-03-1998
		AU 5797496 A	29-11-1996
		CA 2221623 A1	21-11-1996
		EP 0830448 A1	25-03-1998
		JP 11511654 T	12-10-1999
		WO 9636696 A1	21-11-1996